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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/734,443 10/17/96 KEYT

B A-63096/WHD

EXAMINER

HM22/0212

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ART UNIT

PAPER NUMBER

1647
DATE MAILED:

02/12/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/734,443

Applicant(s)

KEYT et al.

Examiner

Christine J. Saoud

Group Art Unit

1647



☒ Responsive to communication(s) filed on Nov 20, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-14 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-4 and 7-14 is/are rejected.

☒ Claim(s) 5 and 6 is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Response to Amendment

1. Claims 1-14 are pending in the instant application.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.
4. Applicant's arguments filed 20 November 2000 have been fully considered but they are not deemed to be persuasive.

EXAMINER'S NOTE: the previous Office action referenced paper #5 for the rejections of record. This was in error. The correct paper # is #2.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

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make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3 and 7-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for substitution with aspartic acid, does not reasonably provide enablement for any amino acid modification as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The prior art of record identifies VEGF mutants which meet the structural limitations of the instant claims. The art teaches substitution of cysteine residues in VEGF with serine. The prior art specifically exemplifies the cysteine residues of the instant claims (see Claffey and Potgens). Applicant has argued in the art rejection that Potgens teaches that the mutant VEGF proteins are not antagonistic. A review of Potgens confirms that these mutant proteins are not antagonistic (see page 32884, column 2, paragraph 3). However, this evidence also shows that the instant claims are not enabled for their full breadth. As demonstrated in Potgens and Claffey, these cysteine residues are necessary for disulfide bonding and dimerization of the VEGF protein. As stated by Potgens at page 32884, VEGF must dimerize in order to bind to its receptor, and receptor binding is a prerequisite for antagonism. Potgens demonstrates that mutation of the cysteine residues interferes with dimerization and therefore, receptor binding. Therefore, Potgens appears to teach away from mutating these cysteines in order to make an antagonist.

The instant specification discloses mutation of the cysteine residues (specifically at positions 51 and/or 60) result in an antagonistic molecule. This result is unexpected based on the

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teachings of Potgens. Because this result is unexpected, claims limited to this substitution are not anticipated or made obvious by the prior art. However, these results cannot serve as a basis for enablement of the broad claim, because evidence of Potgens demonstrates that not each and every amino acid substitution or amino acid modification will result in an antagonist. It is not clear which amino acid substitutions or amino acid modifications would provide for the desired biological activity. The specification only provides guidance for aspartic acid substitution and the art would suggest that it would be unpredictable to substitute other amino acids in light of the result with serine substitution. Therefore, the experimentation that would be required to practice the full breadth of the claims would be undue because one would not have a reasonable expectation of making a substitution or modification, expect for the substitution of aspartic acid, and obtain a functional protein with the required biological activity.

One could argue that substitutions could be made and the resultant protein could be tested for biological activity. However, this is merely an invitation to experiment. Such a suggestion is found in Potgens (see page 32884, column 2, paragraph 3), however, this cannot serve as a basis for a rejection over the prior art and it therefore, cannot serve as a basis for allowance of the generic claim either.

Conclusion

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7. Claims 5-6 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556. If this number is out of service, please call the Group receptionist for an alternate number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

February 9, 2001

**CHRISTINE J. SAOUD
PRIMARY EXAMINER**

Christine J. Saoud